

REMARKS

This paper is filed in response to the official action dated September 14, 2006 (hereafter, the official action). This paper is timely-filed as it is accompanied by a petition for an extension of time to file in the second month and a check covering the requisite fee of \$450.00.

Claims 1-12 are pending. Claims 1-12 have been objected to as not being amended to be drawn to the elected invention. The claims have been amended to address this objection, and therefore this objection has been overcome and should be withdrawn. Specifically, claims 1 and 6 have been amended to recite an amino acid sequence consistent with applicants' election; claims 2 and 3 have been canceled without prejudice or disclaimer in view of applicants' election; and, claim 10 has been amended to be consistent with applicants' election.

Claims 1 and 4 have also been amended to correct a typographical error.

All pending claims 1-12 have been rejected under 35 U.S.C. §103(a) as obvious over Mühlradt *et al.*, *J. Exp. Med.*, 185:1951-1958 (1997) in view of international patent publication no. WO 98/27110 and U.S. Patent No. 4,916,118 to Fidler *et al.* Claims 1-3 and 10-12 have been provisionally rejected for obviousness-type double patenting over claims 1-3, 6-8, 10, and 11 of copending patent application serial no. 10/509,917 in view of Mühlradt *et al.*, *J. Exp. Med.*, 185:1951-1958 (1997). All pending claims 1-12 have also been rejected under 35 U.S.C. §112, second paragraph, as indefinite.

In response to the examiner's request for an English language translation of international application no. PCT/EP97/07090, applicants direct the examiner's attention to U.S. Patent No. 6,573,242, which is the U.S. national phase of international application no. PCT/EP97/07090. The supplemental information disclosure statement filed herewith lists U.S. Patent No. 6,573,242, and therefore applicants submit that they have fully complied with the examiner's request.

The various bases for the claim rejections are addressed below in the order presented in the official action. Reconsideration of the application is solicited in view of the following remarks.

CLAIM REJECTIONS – 35 U.S.C. §103

All pending claims 1-12 have been rejected under 35 U.S.C. §103(a) as obvious over Muhlradt *et al.*, *J. Exp. Med.*, 185:1951-1958 (1997) in view of international patent publication no. WO 98/27110 and U.S. Patent No. 4,916,118 to Fidler *et al.* The applicants respectfully traverse the rejections.

A *prima facie* case of obviousness must satisfy three legal requirements. First, there must be some suggestion or motivation, either in the references themselves, or in knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. See M.P.E.P. §2143. These criteria have not been satisfied with respect to all pending claims 1-12.

Claim 1 recites a method of treating a wound in an animal or human comprising administering to said animal or human a pharmaceutical composition comprising a lipopeptide having an asymmetric carbon atom (as shown in the recited formula) having the absolute configuration R when X = S (sulfur).

In contrast, the examiner conceded that “Muhlradt et al. places no import as to the lipopeptide/lipoprotein structure * asymmetric carbon atom has the absolute configuration R when X = S (sulfur)” Accordingly, this document does not supply any motivation to administer a lipopeptide having an asymmetric carbon atom (as shown in the recited formula) having the absolute configuration R when X = S (sulfur).

Further, although international patent publication no. WO 98/27110 claims a “S-(2,3-dihydroxypropyl) cysteine peptide,” it is silent with respect to the stereo configuration. The applicants submit that one of ordinary skill in the art would understand that the “S” here stands for sulfur, and that the S configuration would have been written as “(S),” if intended. Therefore, this document also does not supply any motivation to administer a lipopeptide having an asymmetric carbon atom (as shown in the recited formula) having the absolute configuration R when X = S (sulfur).

Additionally, Applicants submit that the activity of the lipopeptides or lipoproteins of the claimed invention depends strikingly on the stereo configuration.

In support of this assertion, applicants direct the examiner's attention to Tables 1 and 2 on pages 14 and 15 of the application.

Applicants note that the experimental results reported herein are based on an incorrect interpretation of the stereo configuration of the tested compounds (i.e., the results ascribed to the "R" configuration apply to the "S" configuration and vice versa). Specifically, Example 2 of the present application references a synthetic procedure according to Metzger *et al.* (1991). Metzger *et al.* incorrectly indicated that compounds having the "R" configuration are synthesized using (S)-(-)-glycidol as starting material. Instead, compounds having the "R" configuration are synthesized using (R)-(+)-glycidol as starting material. Thus, in view of Metzger, the applicants mistakenly attributed the results for the "R" configuration to the "S" configuration and vice versa. Nonetheless, applicants had possession of the claimed subject matter at the time of the application filing.

Further, although Mühlradt *et al.* and international patent publication no. WO 98/27110 discuss stimulation of macrophages, they do not disclose successful treating of wounds in animals or humans. Applicants submit that wound healing is a complicated process, and that it cannot be said that an activation of macrophages inevitably leads to a satisfactory wound healing. In support of this assertion, applicants direct the examiner's attention to Eming *et al.*, Am. J. Pathology, 170 (2007) 188, abstract (copy attached hereto as Attachment A):

The impact of the local inflammatory response on the process of wound healing has been debated for decades. In particular, the question whether infiltrating macrophages and granulocytes promote or impede tissue repair has received much attention.

Finally, U.S. Patent No. 4,916,118 to Fidler *et al.* discloses phospholipids compounds comprising phosphate groups. The pending claims do not recite any phosphate containing compounds. Accordingly, one of ordinary skill would not be motivated to modify Mühlradt *et al.* or international patent publication no. WO 98/27110 in view of this reference.

Accordingly, the applicants respectfully submit that a *prima facie* case of obviousness has not been established, and that the outstanding obviousness rejections of claims 1-12 have been overcome and should be withdrawn.

CLAIM REJECTIONS – DOUBLE PATENTING

The applicants will address this provisional rejection if and when it should become mature.

CLAIM REJECTIONS – 35 U.S.C. §112

All pending claims 1-12 have also been rejected under 35 U.S.C. §112, second paragraph, as indefinite.¹

Applicants have amended the claims to address the examiner's concerns, but submit that SEQ ID NO:7 falls within the scope of claim 1 because the racemic mixture of SEQ ID NO:7 necessarily comprises a lipoprotein with the (R) configuration recited by claim 1.

CONCLUSION

It is submitted that the application is in condition for allowance. Should the examiner wish to discuss any matter of form or procedure in an effort to advance this application to allowance, she is respectfully invited to telephone the undersigned attorney at the indicated telephone number.

Respectfully submitted,

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¹ It appears that the examiner mistakenly referenced SEQ ID NO: 10 instead of SEQ ID NO: 8 when stating that 'SEQ ID NO: 10 is indefinite, since it appears to be in the absolute configuration S when X is S...' at page 8 of the official action.



ATTACHMENT A

(*American Journal of Pathology*. 2007;170:188-202.)

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Accelerated Wound Closure in Mice Deficient for Interleukin-10

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The impact of the local inflammatory response on the process of wound healing has been debated for decades. In particular, the question whether infiltrating macrophages and granulocytes promote or impede tissue repair has received much attention. In the present study, we show that wound healing is accelerated in mice deficient for the anti-inflammatory cytokine interleukin (IL)-10. IL-10^{-/-} mice closed excisional wounds significantly earlier compared with IL-10-competent control littermates. This effect was attributable to accelerated epithelialization as well as enhanced contraction of the wound tissue in the mutant animals. Increased α -smooth muscle actin expression in IL-10-deficient mice suggests that augmented myofibroblast differentiation is responsible for the enhanced contraction of wounds in mutant mice. The number of macrophages infiltrating the wound tissue was significantly increased in IL-10^{-/-} mice compared with control littermates suggesting that this cell type mediates the accelerated tissue repair. These results show for the first time that IL-10 can impede wound repair.